CLAIMS

We claim:

1. An isolated caspase or procaspase expressed in immature thymocytes, or an active derivative or fragment thereof, wherein said caspase is necessary for apoptosis.

2. An isolated caspase according to Claim 1, wherein said caspase is characterized by its ability to be triggered by TCR stimulation with peptide/MHC, anti-CD3ε or other anti-TCR-specific monoclonal antibody, or corticosteroids in thymocytes.

3. The isolated caspase or procaspase of Claim 1, wherein said caspase is a fragment possessing caspase activity.

4. The isolated caspase or procaspase of Claim 1, wherein said caspase or procaspase is a derivative possessing substantial sequence identity with the endogenous caspase or procaspase.

5. The isolated caspase or procaspase of Claim 1, wherein said caspase or procaspase has the same amino acid sequence as the endogenous caspase or procaspase.

6. The isolated caspase or procaspase of Claim 5, wherein said caspase or procaspase is isolated from immature thymocytes.

7. The isolated caspase or procaspase of Claim 6, wherein said caspase or procaspase is purified to homogeneity.

8. The isolated caspase or procaspase of Claim 6, wherein said caspase or procaspase is substantially free of other thymocyte proteins.

9. An isolated nucleic acid molecule which encodes a caspase or procaspase expressed in immature thymocytes and necessary for apoptosis, or an active derivative or fragment thereof.

10. An isolated nucleic acid molecule according to Claim 9, wherein the caspase is characterized by its ability to be triggered by TCR stimulation with peptide/MHC, anti-CD3ε or other anti-TCR-specific monoclonal antibody, or corticosteroids in thymocytes.

11. The isolated nucleic acid molecule of Claim 9, wherein said molecule comprises at least about 25 nucleotides.

12. The isolated nucleic acid molecule of Claim 9, wherein said molecule comprises at least about 50 nucleotides.

13. The isolated nucleic acid molecule of Claim 9, wherein said molecule comprises at least about 200 nucleotides.

14. The isolated nucleic acid molecule of Claim 9, wherein the caspase or procaspase is a derivative possessing substantial sequence identity with the endogenous caspase or procaspase.

15. The isolated nucleic acid molecule Claim 9, wherein said caspase or procaspase has the same amino acid sequence as the endogenous caspase or procaspase.

16. The isolated nucleic acid molecule Claim 15, wherein said nucleic acid molecule has the same nucleotide sequence as the endogenous gene encoding the caspase or procaspase.

17. A DNA construct comprising the isolated nucleic acid molecule of Claim 9 operatively linked to a regulatory sequence.

18. A DNA construct comprising the isolated nucleic acid molecule of Claim 15 operatively linked to a regulatory sequence.

19. A DNA construct comprising the isolated nucleic acid molecule of Claim 16 operatively linked to a regulatory sequence.

20. A recombinant host cell comprising the isolated nucleic acid molecule of Claim 9 operatively linked to a regulatory sequence.

21. A recombinant host cell comprising the isolated nucleic acid molecule of Claim 15 operatively linked to a regulatory sequence.

22. A recombinant host cell comprising the isolated nucleic acid molecule of Claim 16 operatively linked to a regulatory sequence.

23. The recombinant host cell of Claim 22 wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, insect cells and mammalian cells.

24. A method for preparing a caspase or procaspase expressed in immature thymocytes, or an active derivative or fragment thereof, wherein said caspase is necessary for apoptosis, comprising culturing the recombinant host cell of Claim 20.

25. A method according to Claim 24, wherein the caspase is characterized by its ability to be triggered by TCR stimulation with peptide/MHC, anti-CD3ε or other anti-TCR-specific monoclonal antibody, or corticosteroids in thymocytes

26. An antibody, or an antigen-binding fragment thereof, which selectively binds to the caspase or procaspase according to Claim 1, or an active derivative or fragment thereof.

27. The antibody according to Claim 26, wherein said antibody is a monoclonal antibody.

28. A method for assaying the presence of a caspase or procaspase according to Claim 1 in a cell, comprising contacting said cell with an antibody which specifically binds to the caspase or procaspase.

29. The method of Claim 28, wherein said cell is in a tissue sample.

30. A method of identifying an agent which inhibits the caspase according to Claim 1, comprising the steps of:

(a) contacting the caspase, or an active derivative or fragment thereof, with a

caspase substrate in the presence of the agent; and

(b) identifying inhibition of caspase activity.

31. An agent which inhibits caspase activity identified according to the method of Claim 30.

32. A method of identifying an agent which inhibits the caspase according to Claim 1, comprising the steps of:

(a) contacting a thymocyte or a cell lysate thereof comprising the caspase or procaspase with the agent; and

(b) identifying inhibition of caspase activity.

33. An agent which inhibits caspase activity identified according to the method of Claim 32.

34. A method of inhibiting the caspase according to Claim 1, comprising contacting said caspase with an agent that inhibits the activity of the caspase.

35. A method of inhibiting apoptosis in a lymphocyte comprising contacting said lymphocyte with an agent which inhibits the caspase according to Claim 1.

36. A method according to Claim 35, wherein said apoptosis is induced by a member of the group consisting of an antigen, a corticosteroid and anti-CD3ϵ monoclonal antibody.

37. A method according to Claim 35, wherein the lymphocyte is an immature thymocyte.

38. A method according to Claim 35, wherein the agent is a tripeptide or tetrapeptide having an amino acid sequence selected from the group consisting of VAD, YVAD, and DEVD, and wherein the tetrapeptide or tripeptide is linked to a compound selected from the group consisitng of fluoromethylketone, acyloxymethylketone, chlormethylketone, diazomethylketone, aldehydes, semicarbazones, nitriles and epoxides.

39. A method of inhibiting apoptosis in an immature thymocyte comprising contacting said thymocyte with an agent according to Claim 31.

40. A method of inhibiting apoptosis in an immature thymocyte comprising contacting said thymocyte with an agent according to Claim 33.

41. A method of identifying an agent which enhances the caspase according to Claim 1, comprising the steps of:

(a) contacting the caspase, or an active derivative or fragment thereof, with a caspase substrate in the presence of the agent; and

(b) identifying enhancement of caspase activity.

42. An agent which enhances caspase activity identified according to the method of Claim 41.

43. A method of identifying an agent which enhances the caspase according to Claim 1, comprising the steps of:

(a) contacting a thymocyte or a cell lysate thereof comprising the caspase or procaspase, with the agent; and

(b) identifying enhancement of caspase activity.

44. An agent which enhances caspase activity identified according to the method of Claim 43.

45. A method of enhancing the caspase according to Claim 1, comprising contacting said caspase with an agent that enhances the activity of the caspase.

46. A method of enhancing apoptosis in a lymphocyte comprising contacting said lymphocyte with an agent which enhances the caspase according to Claim 1.

47. A method according to Claim 46, wherein the lymphocyte is an immature thymocyte.

48. A method of enhancing apoptosis in an immature thymocyte comprising contacting said thymocyte with an agent according to Claim 42.

49. A method of treating an autoimmune disease in a mammal comprising administering to the mammal an effective amount of an agent which enhances the activity of the caspase according to Claim 1.

50. The method of Claim 49, wherein the autoimmune disease is chronic hepatitis or diabetes mellitus.

51. A method of enhancing an immune response against an antigen in a mammal comprising administering to the mammal an effective amount of an agent which inhibits the activity of the caspase according to Claim 1 and an antigen.

52. A method of treating a cancer in a mammal comprising administering to the mammal an effective amount of an agent which inhibits the activity of the caspase according to Claim 1 and a cancer antigen.